

Application No.: 10/646,070

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Resp to Restriction Requirement of 10/15/04

**AMENDMENTS TO THE CLAIMS**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

Claims 1-47 (canceled).

Claim 48 (currently amended): An isolated genetic construct,  
wherein said genetic construct is capable of post-transcriptionally delaying, repressing or otherwise reducing the expression of a target gene in a human cell transfected with the genetic construct by sequence-specific degradation of a RNA transcript of the target gene by an endogenous system of the human cell,

wherein the genetic construct comprises at least two copies of a structural gene sequence,  
wherein the structural gene sequence comprises a nucleotide sequence which is ~~substantially~~  
at least 80% identical to at least a region the sequence of the target gene or region thereof,

wherein the at least two copies of the structural gene sequence are placed operably under the control of at least one promoter which is operable in the human cell, and

wherein at least one copy of the structural gene sequence is placed operably in the sense orientation under the control of the at least one promoter.

Claim 49 (currently amended): An isolated genetic construct,  
wherein said genetic construct is capable of post-transcriptionally delaying, repressing or otherwise reducing the expression of a target gene in a human cell transfected with the genetic construct by sequence-specific degradation of a RNA transcript of the target gene by an endogenous system of the human cell,

wherein the genetic construct comprises at least two copies of a structural gene sequence,  
wherein each copy of said structural gene sequence is separately placed under the control of a promoter which is operable in the human cell,

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wherein each copy of said structural gene sequence comprises a nucleotide sequence which is substantially at least 80% identical to at least a region the sequence of the target gene or region thereof,

and wherein at least one copy of the structural gene sequence is placed operably in the sense orientation under the control of an individual promoter sequence.

Claim 50 (previously presented): The isolated genetic construct of claim 48 wherein at least one other copy of the structural gene sequence is placed operably in the antisense orientation under the control of the promoter.

Claim 51 (currently amended): An isolated genetic construct, wherein said genetic construct is capable of post-transcriptionally delaying, repressing or otherwise reducing the expression of a target gene in a human cell transfected with the genetic construct by sequence-specific degradation of a RNA transcript of the target gene by an endogenous system of the human cell,

wherein the genetic construct comprises at least two copies of a structural gene sequence, wherein the structural gene sequence comprises a nucleotide sequence which is substantially at least 80% identical to at least a region the sequence of the target gene or region thereof,

wherein at least one copy of the structural gene sequence is placed under the control of a first promoter operable in the human cell and at least one other copy of the structural gene is placed under the control of a second promoter operable in the human cell, and

wherein at least one copy of the structural gene sequence is placed operably in the sense orientation under the control of either said first or second promoter.

Claim 52 (previously presented): The isolated genetic construct of claim 49 wherein at least one other copy of the structural gene sequence is placed operably in the antisense orientation under control of the second promoter.

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Claim 53 (currently amended): The isolated genetic construct of claim 50, wherein said at least one copy of the structural gene sequence that is placed in the sense orientation relative to the promoter and said at least one other copy of the structural gene sequence that is placed in the antisense orientation relative to the promoter are ~~spaced from each other~~ separated by a nucleic acid containing stuffer fragment.

Claim 54 (previously presented): The isolated genetic construct of claim 53, wherein the nucleic acid stuffer fragment is above about 10 and below about 50 nucleic acids in length.

Claim 55 (previously presented): The isolated genetic construct of claim 52, wherein transcription of the two or more copies of the structural gene sequences produces at least two single stranded RNA transcripts which hybridize to form double stranded RNA.

Claim 56 (previously presented): The isolated genetic construct of claim 52, wherein the first and second promoters are selected from the group consisting of a T7 promoter, a T3 promoter, a SP6 promoter, a *lac* operator-promoter, a *tac* promoter, an SV40 late promoter, an SV40 early promoter, an RSV-LTR promoter and a CMV IE promoter.

Claim 57 (previously presented): The isolated genetic construct of claim 56 wherein at least one of the first and second promoters is a T7 promoter.

Claim 58 (previously presented): The isolated genetic construct according to claim 48, wherein the structural gene sequence comprises a nucleotide sequence that is identical to the region of the target gene.

Claim 59 (previously presented): The isolated genetic construct according to claim 51, wherein the structural gene sequence comprises a nucleotide sequence that is identical to the region of the target gene.

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**Claim 60 (previously presented):** An isolated human cell comprising the genetic construct of claim 48.

**Claim 61 (previously presented):** An isolated human cell comprising the genetic construct of claim 51.

**Claim 62 (previously presented):** The isolated genetic construct according to claim 48 wherein the region of the target gene is about 20 to 30 nucleotides in length.

**Claim 63 (previously presented):** The isolated genetic construct according to claim 51 wherein the region of the target gene is about 20 to 30 nucleotides in length.

**Claim 64 (previously presented):** The isolated genetic construct according to claim 48, further comprising a viral vector.

**Claim 65 (previously presented):** The isolated genetic construct according to claim 64, wherein the viral vector is selected from the group consisting of a retrovirus and a lentivirus.

**Claim 66 (previously presented):** The isolated genetic construct according to claim 51, further comprising a viral vector.

**Claim 67 (previously presented):** The isolated genetic construct according to claim 66, wherein the viral vector is selected from the group consisting of a retrovirus and a lentivirus.

**Claim 68 (previously presented):** The isolated genetic construct according to claim 48 wherein the target gene is from a viral pathogen of the human cell.

**Claim 69 (previously presented):** The isolated genetic construct according to claim 49 wherein the target gene is from a viral pathogen of the human cell.

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**Claim 70 (previously presented):** The isolated genetic construct according to claim 68 wherein the viral pathogen is a lentivirus or a retrovirus.

**Claim 71 (previously presented):** The isolated genetic construct according to claim 69 wherein the viral pathogen is a lentivirus or a retrovirus.

**Claim 72 (previously presented):** An isolated genetic construct according to claim 48 wherein the region of the target gene encodes an amino acid sequence.

**Claim 73 (previously presented):** An isolated genetic construct according to claim 51 wherein the region of the target gene encodes an amino acid sequence.

**Claim 74 (previously presented):** An isolated genetic construct according to claim 48 wherein the region of the target gene does not encode an amino acid sequence.

**Claim 75 (previously presented):** An isolated genetic construct according to claim 51 wherein the region of the target gene does not encode an amino acid sequence.

**Claim 76 (previously presented):** The isolated genetic construct according to claim 48 wherein the target gene is  $\alpha$ -1,3-galactosyltransferase.

**Claim 77 (previously presented):** The isolated genetic construct according to claim 51 wherein the target gene is  $\beta$ -1,3-galactosyltransferase.

**Claim 78 (previously presented):** The isolated genetic construct according to claim 48 wherein the target gene is derived from the genome of a pathogen of the human cell or the genome of the human cell.

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**Claim 79 (previously presented):** The isolated genetic construct according to claim 51 wherein the target gene is derived from the genome of a pathogen of the human cell or the genome of the human cell.

**Claim 80 (previously presented):** The isolated genetic construct according to claim 78 wherein the pathogen is a virus.

**Claim 81 (previously presented):** The isolated genetic construct according to claim 79 wherein the pathogen is a virus.

**Claim 82 (currently amended):** An isolated genetic construct according to claim 48 wherein the target gene is endogenous to the genome of the human cell.

**Claim 83 (currently amended):** An isolated genetic construct according to claim 51 wherein the target gene is endogenous to the genome of the human cell.

**Claim 84 (currently amended):** An isolated genetic construct according to claim 48 wherein the target gene is exogenous to the genome of the human cell.

**Claim 85 (currently amended):** An isolated genetic construct according to claim 51 wherein the target gene is exogenous to the genome of the human cell.

**Claim 86 (previously presented):** An isolated genetic construct according to claim 48 comprising two copies of said structural gene sequence.

**Claim 87 (previously presented):** An isolated genetic construct according to claim 51 comprising two copies of said structural gene sequence.

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**Claim 88 (previously presented):** A pharmaceutical composition comprising an isolated genetic construct according to claim 48 and further including an active ingredient.

**Claim 89 (previously presented):** A pharmaceutical composition comprising an isolated genetic construct according to claim 51 and further including an active ingredient.

**Claim 90 (previously presented):** A pharmaceutical composition comprising an isolated genetic construct according to claim 48 and a pharmaceutically acceptable carrier, excipient or diluent.

**Claim 91 (previously presented):** A pharmaceutical composition comprising an isolated genetic construct according to claim 51 and a pharmaceutically acceptable carrier, excipient or diluent.

**Claim 92 (previously presented):** A method of treating a human cell in need of treatment, comprising:  
administering the genetic construct of claim 48 to said human cell.

**Claim 93 (previously presented):** A method of treating a human cell in need of treatment, comprising:  
administering the genetic construct of claim 51 to said human cell.

**Claim 94 (previously presented):** The method of claim 92, wherein said administering step further comprises transient transfection of said cell.

**Claim 95 (previously presented):** The method of claim 93, wherein said administering step further comprises transient transfection of said cell.

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**Claim 96 (previously presented):** The method of claim 92, wherein said administering step further comprises stable transfection of said cell.

**Claim 97 (previously presented):** The method of claim 93, wherein said administering step further comprises stable transfection of said cell.

**Claim 98 (previously presented):** A method for treating a human in need of treatment, comprising  
administering the genetic construct of claim 48 to said human.

**Claim ~~99~~98 (currently amended):** A method of treating a human in need of treatment, comprising administering the genetic construct of claim 49 to said human.

**Claim 100 (previously presented):** The method of claim 92, further comprising administering the genetic construct of claim 48 together with a suitable carrier, excipient and/or diluent to said human.

**Claim 101 (previously presented):** The method of claim 93, further comprising administering the genetic construct of claim 48 together with a suitable carrier, excipient and/or diluent to said human.

**Claim 102 (previously presented):** A method for treating a human in need of treatment, comprising:  
taking the cell from said human;  
transfecting the cell with the genetic construct of claim 48  
replacing the cell in the human.

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**Claim 103 (previously presented):** A method for treating a human in need of treatment, comprising:

taking the cell from said human;

transfecting the cell with the genetic construct of claim 51; and

replacing the cell in the human.

**Claim 104 (previously presented):** The method of claim 103, wherein transcription of the one or more copies of the structural gene sequences produces two single stranded RNA transcripts which hybridize to form double stranded RNA.

**Claim 105 (previously presented):** A method of treating a human cell in need of treatment, comprising: administering the pharmaceutical composition of claim 88 to said human cell.

**Claim 106 (previously presented):** A method of treating a human cell in need of treatment, comprising: administering the pharmaceutical composition of claim 89 to said human cell.

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